Groups 19-22 corresponding to claim 19; and Groups 23-26 corresponding to claim 19. Groups 1-4 is further restricted to a specific sequence (e.g., SEQ ID No. 2, 4, 6 or 8) to which the claims are to be drawn for examination.

Applicants respectfully elect Groups 1-4 and elect sequence SEQ ID No. 8 without traverse. Applicants have also added claims 20-35 directed to various methods of detecting the presence of specific immunological complexes formed between a polypeptide in the diagnosing of a tumor of cancerous origin such as the diagnosis of paraneoplastic syndrome. Specifically, the added claims include various methods of diagnostics comprising contacting a sample with a polypeptide, derivative, or fragment thereof. Such uses were identified by the Examiner as corresponding to Groups 1-4.

In short, all new claims are drawn to the use of a POP-66 polypeptide for diagnostic purposes and therefore directly relate to Claims 9, 10, 14 and 15. These claims involve the recognition of endogenous antibodies by means of a POP-66 polypeptide. Accordingly, added claims 20-35 should be included as claims corresponding to elected Groups 1-4.

Respectfully submitted,

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ATTACHMENT A

Clean Amended and New Claims

Following herewith is a clean copy of the entire set of pending claims.

1. Purified polypeptide comprising an amino acid sequence selected from SEQ ID No. 2, No. 4, No. 6 and No. 8.

2. Purified polypeptide according to Claim 1, comprising the amino acid sequence SEQ ID No. 8, the said polypeptide being designated by "POP-66".

3. Isolated nucleotide acid comprising a sequence coding for a polypeptide of amino acid sequence SEQ ID No. 2, No. 4, No. 6 or No. 8.

4. Nucleic acid according to Claim 3, comprising a sequence selected from SEQ ID No. 1, No. 3, No. 5 or No. 7, respectively coding for a polypeptide of amino acid sequence SEQ ID No. 2, No. 4, No. 6 or No. 8.

5. (Amended) Nucleic acid according to Claim 4, comprising the nucleotide sequence SEQ ID No. 7 coding for a comprising the amino acid sequence SEQ ID No. 8, said polypeptide being designated by "POP-66".

a1 encl

6. (Amended) Cloning and/or expression vector containing a nucleic acid sequence according to Claim 3.

7. Host cell transfected by a vector according to Claim 6.

8. Cancelled.

9. Composition useful for the diagnosis of paraneoplastic neurological syndromes and/or for the early diagnosis of the formation of tumours, characterized in that it comprises a purified POP-66 polypeptide, according to Claim 2.

a2

10. (Amended) Use of a purified POP-66 polypeptide according to Claim 2, derivative or biologically active polypeptide fragment of POP-66, or of a nucleic acid comprising the nucleotide sequence of SEQ ID No. 7 for detecting the presence of anti-CV2 antibodies in a biological sample.

11. Cancelled.

12. Cancelled.

13. Cancelled.

14. Method for the diagnosis of paraneoplastic neurological syndromes and/or for the early diagnosis of the formation of cancerous tumours, characterized in that auto-antibodies directed against a POP-66 protein are demonstrated in a blood sample taken from an individual by

- the contacting of a blood sample taken from an individual with a purified polypeptide (POP-66) according to Claim 2, derivative or biologically active polypeptide fragment of POP-66, optionally attached to a support under conditions allowing the formation of specific immunological complexes between the said polypeptide and the auto-antibodies optionally present in the blood sample, and
- the detection of the specific immunological complexes optionally formed.

15. Kit for the diagnosis of paraneoplastic neurological syndromes and for the early diagnosis of the formation of tumours from a biological sample, comprising:

- at least one purified POP-66, according to Claim 2, derivative or biologically active polypeptide fragment of POP-66 polypeptide, optionally attached to a support,
- means of visualization of the formation of specific antigen/antibody complexes between an anti-POP-66 auto-antibody and the said purified POP-66 polypeptide, derivative or polypeptide fragment and/or means of qualification of these complexes.

16. Pharmaceutical composition, comprising at least one purified protein of the ULIP family, polypeptide fragment or biologically active derivative of this, a nucleotide sequence or nucleotide sequence fragment coding for the said protein, an antisense sequence capable of hybridizing specifically with a nucleotide sequence coding for the said protein, or an antibody directed against the said protein, combined with a pharmaceutically acceptable vehicle.

17. (Amended) Pharmaceutical composition according to Claim 15, comprising at least one purified POP-66, polypeptide fragment or biologically active derivative of this, a nucleotide sequence or nucleotide sequence fragment coding for the said polypeptide an antisense sequence capable of hybridizing specifically with a nucleotide sequence coding for the said polypeptide, or an antibody directed against the said polypeptide, combined with a pharmaceutically acceptable vehicle.

A3

18. Cancelled.

19. Cancelled.

20. (New) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising the steps of:

A4

contacting a sample from the subject with a POP-66 polypeptide, said contacting carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of a paraneoplastic syndrome in said subject.

21. (New) The method of claim 20, wherein the polypeptide is the entire POP-66 protein.

22. (New) The method of claim 20, wherein the polypeptide is an antigenic fragment of the POP-66 protein.

23. (New) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising, the steps of:

contacting a sample from the subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with a ULIP polypeptide, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of a paraneoplastic syndrome in said subject.

24. (New) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising the steps of:

contacting a sample from said subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with POP-66, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed between the peptide and antibodies in the sample;

wherein the presence of specific immunological complexes formed between the peptide and antibodies is indicative of a paraneoplastic syndrome in said subject

25. (New) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said subject with a POP-66 polypeptide, said contacting carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of the formation of a tumor in said subject.

26. (New) The method of claim 25, wherein the polypeptide is the entire POP-66 protein.

27. (New) The method of claim 25, wherein the polypeptide is an antigenic fragment of the POP-66 protein.

28. (New) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said, subject with a ULIP polypeptide, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of the formation of a tumor in said subject.

29. (New) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with POP-66, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed between the peptide and antibodies in the sample;

wherein the presence of specific immunological complexes formed between the peptide and antibodies is indicative of the formation of a tumor in said subject.

30. (New) A diagnostic substrate for identifying antibodies to POP-66 in a subject, said substrate comprising:

a solid support; and

a peptide comprising an antigenic portion of POP-66.

31. (New) The substrate of claim 27, wherein the support comprises animal brain, and wherein the antigenic portion of POP-66 is endogenous to said brain.

32. (New) The substrate of claim 27, wherein the antigenic portion of POP-66 is attached to said support.

33. (New) A diagnostic kit for identifying antibodies to POP-66 in a subject, said kit comprising an antigenic portion of POP-66 or a derivative thereof.

34. (New) The kit of claim 29, wherein the kit further comprises means of visualizing formation of POP-66-antibody complexes.

35. (New) The kit of claim 29, wherein the antigenic portion of POP-66 is purified.

ATTACHMENT B

Marked-Up Amended Claims and New Claims

Following herewith is a marked-up copy of the entire set of pending claims.

1. Purified polypeptide comprising an amino acid sequence selected from SEQ ID No. 2, No. 4, No. 6 and No. 8.

2. Purified polypeptide according to Claim 1, comprising the amino acid sequence SEQ ID No. 8, the said polypeptide being designated by "POP-66".

3. Isolated nucleotide acid comprising a sequence coding for a polypeptide of amino acid sequence SEQ ID No. 2, No. 4, No. 6 or No. 8.

4. Nucleic acid according to Claim 3, comprising a sequence selected from SEQ ID No. 1, No. 3, No. 5 or No. 7, respectively coding for a polypeptide of amino acid sequence SEQ ID No. 2, No. 4, No. 6 or No. 8.

5. (Amended) Nucleic acid according to Claim 4, comprising the nucleotide sequence SEQ ID No. 7 coding for a ~~polypeptide according to Claim 2~~comprising the amino acid sequence SEQ ID No. 8, said polypeptide being designated by "POP-66".

6. (Amended) Cloning and/or expression vector containing a nucleic acid sequence according to ~~one of Claims~~ Claim 3 ~~to 5~~.

7. Host cell transfected by a vector according to Claim 6.

8. Cancelled.

9. Composition useful for the diagnosis of paraneoplastic neurological syndromes and/or for the early diagnosis of the formation of tumours, characterized in that it comprises a purified POP-66 polypeptide, according to Claim 2.

10. (Amended) Use of a purified POP-66 polypeptide according to Claim 2, derivative or biologically active polypeptide fragment of POP-66, or of a nucleic acid ~~according to Claim 5~~ comprising the nucleotide sequence of SEQ ID No. 7 for detecting the presence of anti-CV2 antibodies in a biological sample.

11. Cancelled.

12. Cancelled.

13. Cancelled.

14. Method for the diagnosis of paraneoplastic neurological syndromes and/or for the early diagnosis of the formation of cancerous tumours, characterized in that auto-antibodies directed against a POP-66 protein are demonstrated in a blood sample taken from an individual by

- the contacting of a blood sample taken from an individual with a purified polypeptide (POP-66) according to Claim 2, derivative or biologically active polypeptide fragment of POP-66, optionally attached to a support under conditions allowing the formation of specific immunological complexes between the said polypeptide and the auto-antibodies optionally present in the blood sample, and
- the detection of the specific immunological complexes optionally formed.

15. Kit for the diagnosis of paraneoplastic neurological syndromes and for the early diagnosis of the formation of tumours from a biological sample, comprising:

- at least one purified POP-66, according to Claim 2, derivative or biologically active polypeptide fragment of POP-66 polypeptide, optionally attached to a support,
- means of visualization of the formation of specific antigen/antibody complexes between an anti-POP-66 auto-antibody and the said purified POP-66 polypeptide, derivative or polypeptide fragment and/or means of qualification of these complexes.

16. Pharmaceutical composition, comprising at least one purified protein of the ULIP family, polypeptide fragment or biologically active derivative of this, a nucleotide sequence or nucleotide sequence fragment coding for the said protein, an antisense sequence capable of hybridizing specifically with a nucleotide sequence coding for the said protein, or an antibody directed against the said protein, combined with a pharmaceutically acceptable vehicle.

17. (Amended) Pharmaceutical composition according to Claim 15, comprising at least one purified POP-66 ~~polypeptide according to Claim 2~~, polypeptide fragment or biologically active derivative of this, a nucleotide sequence or nucleotide sequence fragment coding for the said polypeptide an antisense sequence capable of hybridizing specifically with a nucleotide sequence coding for the said polypeptide, or an antibody directed against the said polypeptide, combined with a pharmaceutically acceptable vehicle.

18. Cancelled.

19. Cancelled.

20. (New) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising the steps of:

contacting a sample from the subject with a POP-66 polypeptide, said contacting carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of a paraneoplastic syndrome in said subject.

21. (New) The method of claim 20, wherein the polypeptide is the entire POP-66 protein.

22. (New) The method of claim 20, wherein the polypeptide is an antigenic fragment of the POP-66 protein.

23. (New) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising, the steps of:

contacting a sample from the subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with a ULIP polypeptide, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of a paraneoplastic syndrome in said subject.

24. (New) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising the steps of:

contacting a sample from said subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with POP-66, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed between the peptide and antibodies in the sample;

wherein the presence of specific immunological complexes formed between the peptide and antibodies is indicative of a paraneoplastic syndrome in said subject

25. (New) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said subject with a POP-66 polypeptide, said contacting carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of the formation of a tumor in said subject.

26. (New) The method of claim 25, wherein the polypeptide is the entire POP-66 protein.

27. (New) The method of claim 25, wherein the polypeptide is an antigenic fragment of the POP-66 protein.

28. (New) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said, subject with a ULIP polypeptide, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of the formation of a tumor in said subject.

29. (New) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a

specific immunological complex with POP-66, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed between the peptide and antibodies in the sample;

wherein the presence of specific immunological complexes formed between the peptide and antibodies is indicative of the formation of a tumor in said subject.

30. (New) A diagnostic substrate for identifying antibodies to POP-66 in a subject, said substrate comprising:

a solid support; and

a peptide comprising an antigenic portion of POP-66.

31. (New) The substrate of claim 27, wherein the support comprises animal brain, and wherein the antigenic portion of POP-66 is endogenous to said brain.

32. (New) The substrate of claim 27, wherein the antigenic portion of POP-66 is attached to said support.

33. (New) A diagnostic kit for identifying antibodies to POP-66 in a subject, said kit comprising an antigenic portion of POP-66 or a derivative thereof.

34. (New) The kit of claim 29, wherein the kit further comprises means of visualizing formation of POP-66-antibody complexes.

35. (New) The kit of claim 29, wherein the antigenic portion of POP-66 is purified.